

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US03/27888

**A. CLASSIFICATION OF SUBJECT MATTER**

IPC(7) : A61K 35/00, 48/00; C07K 5/00, 14/00; C12N 15/85, 15/86  
US CL : 424/93.1; 435/325; 514/44; 530/300, 350, 399

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 424/93.1; 435/325; 514/44; 530/300, 350, 399

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Continuation Sheet

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,891,558 A (BELL et al.) 06 April 1999 (06.04.1999), Cols. 4-19.	1-91
X	US 5,855,617 A (ORTON) 05 January 1999 (05.01.1999), Cols. 4-6.	1-91
X	US 5,863,296 A (ORTON) 26 January 1999 (26.01.1999), Cols. 4-7.	1-91
X,P	US 2003/0064927 A1 (GESTRELIUS et al.) 03 April 2003 (03.04.2003), Examples 1-9.	1-91
X,P	US 2003/0166274 A1 (HEWITT et al.) 04 September 2003 (04.09.2003), Examples I-IX.	1-91
X	COOPER, M.L. et al. Use of a composite skin graft composed of cultured human keratinocytes and fibroblasts and a collagen-GAG matrix to cover full-thickness wounds on athymic mice. Surgery. February 1991, Vol. 109, No. 2, pages 198-207, especially Figures 1 and 4, Table I.	1-91

Further documents are listed in the continuation of Box C.

See patent family annex.

• Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Z"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

31 October 2003 (31.10.2003)

Date of mailing of the international search report

04 DEC 2003

Name and mailing address of the ISA/US

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## INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LANGDON, R.C. et al. Reconstitution of Structure and Cell Function in Human Skin Grafts Derived from Cryopreserved Allogeneic Dermis and Autologous Cultured Keratinocytes. <i>J Invest Dermatol.</i> November 1988, Vol. 91, No. 5, pages 478-485, especially Figures 1-4.	1-91
X	SUGIHARA, H. et al. Effects of fat cells on keratinocytes and fibroblasts in a reconstructed rat skin model using collagen gel matrix culture. <i>British Journal of Dermatology.</i> 2001, Vol. 144, pages 244-253, especially Figures 1 and 2.	1-91
X	KOLODKA, T.M. et al. Evidence for keratinocyte stem cells in vitro: Long term engraftment and persistence of transgene expression from retrovirus-transfected keratinocytes. <i>Proc. Natl. Acad. Sci., USA.</i> April 1998, Vol. 95, pages 4356-4361, especially Table 1 and 2.	1-91
X	BADIAVAS, E. et al. Retrovirally mediated gene transfer in a skin equivalent model of chronic wounds. <i>Journal of Dermatological Science.</i> 1996, Vol. 13, pages 56-62, especially Figure 3.	1-91
X	MARUGUCHI, T. et al. A new skin equivalent: Keratinocytes proliferated and differentiated on collagen sponge containing fibroblasts. <i>Plast. Reconstr. Surg.</i> March 1994, Vol. 93, No. 3, pages 537-546, especially Figures 1-4.	1-91
A,P	US 2002/0169105 A1 (GESTRELIUS et al.) 14 November 2002 (14.11.2002), entire document.	1-91
A	US 2002/0031500 A1 (MACLAUGHLIN et al.) 14 March 2002 (14.03.2002), entire document.	1-91
A	KUROYANAGI, Y. et al. A cultured skin substitute composed of fibroblasts and keratinocytes with a collagen matrix: Preliminary results of clinical trials. <i>Ann Plast Surg.</i> October 1993, Vol. 31, No. 4, pages 340-351, entire document.	1-91
A	DEL RIO, M. et al. A preclinical model for the analysis of genetically modified human skin in vivo. <i>Human Gene Therapy.</i> 20 May 2002, Vol. 13, No. 8, pages 959-968, entire document.	1-91
A	CURRIE, L.J. et al. The use of fibrin glue in skin grafts and tissue-engineered skin replacements: A Review. <i>Plast Reconstr Surg.</i> November 2001, Vol. 108, No. 6, pages 1713-1726, entire document.	1-91

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**Continuation of B. FIELDS SEARCHED Item 3:**

WEST (USPT, PGPUBS, JPO, EPO, DERWENT); NCBI (PUBMED); STN (BIOSCIENCE)  
fibroblast, keratinocyte, differentiated, differentiation, fibrin, collagen, matrix, allogeneic, epithelial, blood, mitomycin C, X-ray,  
scaffold, wound dressing, T antigen, EBV, HTLV-1, EBNA2, glycerol, c-myc, c-kun. myc, n-myc